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10/527,090	03/10/2005	Kensuke Yuuki	050148	1836

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EXAMINER

CHOWDHURY, IQBAL HOSSAIN

ART UNIT PAPER NUMBER

1652

DATE MAILED: 08/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/527,090	Applicant(s) YUUKI ET AL.	
	Examiner Iqbal Chowdhury, Ph.D.	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 May 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10/05</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

In response to a previous Office action, a non-final requirement (mailed on February 8, 2006), Applicants filed a response and amendment received on May 5, 2006. Applicant's amendment of claims 1-24 and newly adding claims 25-36 has been entered. Claims 1-36 are pending in the instant Office action and will be examined herein.

Applicants' arguments filed on 5/5/2006 have been fully considered and are not deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Withdrawn -Claim Objections

Previous objection of Claims 7 and 19 is withdrawn by virtue of applicant's amendments of claims.

Withdrawn-Claim Rejections - 35 U.S.C. § 112(2)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Previous rejection of Claim 1-4, 6, 7-16, and 18-24 under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn by virtue of applicants amendments of the claims and arguments. Applicants changed the statement of "derived from Streptomyces" to "isolated from Streptomyces"

Previous rejection of Claim 6, 12, 18 and 24 under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn by virtue of applicants amendments of the claims and arguments. The recitation "or a mutant strain thereof" has been deleted.

New-Claim Rejections - 35 U.S.C. § 112(2)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 25-26, 28-29, 31-32, and 34-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 25-26, 28-29, 31-32, and 34-35 are indefinite and vague in the recitation of the "sequence hybridizes to DNA of SEQ ID ---- under conditions of 50% formaldehyde, 10X SSC---", which is ambiguous and confusing. Formaldehyde is not a constituent of hybridizing solution rather a fixing solution of protein. The hybridizing solution usually comprises 50% formamide. Clarification is required.

Maintained - Claim Rejections - 35 U.S.C. § 112 (1)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Previous rejection of claims 1-3, 6-9, 12-15, 18-21, 24 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. This

rejection has been discussed at length in the previous office action mailed on 2/8/2006. It is maintained for the reasons of record and discussed below.

These claims are directed to a wild type or mutant strains of *Streptomyces* (*S.*) *mobaraensis* or *S. lividans* comprising any wild type *S. mobaraensis* transglutaminase, cloning in an expression vector with promoter and terminator for expression of the polypeptide and collecting the produced transglutaminase.

The specification teaches the structure of only two representative species of such DNAs used to produce transformed wild type strains. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding any transglutaminase gene to be used to produce transformed wild type and mutant strains. Given this lack of description of representative species encompassed by the genus of DNAs used to produce transformed wild type or mutant strains, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicants argue various matters including “derived” vs. “isolated” of transglutaminase gene or “mutant strains” or “sequence obtained by modifying” etc, however, the issue of these claims is lack of structural feature of the claimed genus. Applicants have not provided any structural features of the claimed genus in these claims.

Applicant’s arguments have been fully considered but are not deemed persuasive to overcome the rejection of claims 1-3, 6-9, 12-15, 18-21, 24. The main issue to satisfy the written description requirement is having clear picture of structure and function of the claimed genus.

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These claims do not have any structural feature, which read a transformant comprising any transglutaminase gene.

Therefore, for the reasons above, the rejection of claims 1-3, 6-9, 12-15, 18-21, and 24 are maintained.

Previous rejection of claims 1-3, 6-9, 12-15, 18-21, 24 under 35 U.S.C. 112, first paragraph, on Scope of Enablement issue is maintained. This previous rejection has been fully discussed at length in the previous office action mailed on 2/8/2006. It is maintained for the reasons of record and discussed below.

These claims are so broad as to encompass any transformant of *S. mobaraensis* or *S. lividans* strains comprising any gene encoding any wild type transglutaminase from *S. mobaraensis*, cloning in an expression vector with promoter and terminator with unknown structure for expression of the polypeptide (wild type or mutant) in the said bacterial strains and collecting the produced transglutaminase. The scope of the methods claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of genes encoding transglutaminase protein broadly encompassed by the claims. The scope of the claimed invention is very broad in the context of lack of structural feature of the gene encoding polypeptide.

Applicants argue that the gene of transglutaminase in amended claims 1-3, 7-9, 13-15 and 19-21, reads only on the gene of transglutaminase isolated from specific strains, and one of skill in the art can obtain these genes. Similarly, new claims 27, 30, 33 and 36 are product-by-process claims, and one of skill in the art can mutate the recited strains. Applicants also submit that new

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claims 25-36 are fully enabled by the specification; in particular, new claims 25, 26, 28, 29, 31, 32, 34 and 35, recite transformants having structural genes comprising a sequence obtained by modifying SEQ ID N0: 1 (or SEQ ID N0: 2), with the scope of the modification being defined by the specifically recited hybridization parameters. Applicants also argue that the given hybridization parameters allow one of skill in the art to obtain sequences within the scope of the claim by standard techniques and without experimentation.

Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection of claims 1-3, 6-9, 12-15, 18-21, 24 on Scope of Enablement issue. The examiner acknowledges the amendment to the claims and adding new claims by providing more limitation but disagrees with the applicant's contention that the scope of the claimed invention is adequately enabled. Claims 1-3, 6-9, 12-15, 18-21, 24 are directed to a wild type or mutant strains of *Streptomyces* (*S.* mobaraensis or *S. lividans* comprising any wild type transglutaminase, cloning in an expression vector with promoter and terminator for expression of the polypeptide and collecting the produced transglutaminase. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to any transformant of *S. mobaraensis* or *S. lividans* strains comprising any wild type transglutaminase gene from *S. mobaraensis* broadly encompassed by the claims.

Applicants have not provided any structural feature of Claims 1-3, 6-9, 12-15, 18-21 and 24. Applicants need to limit the claimed invention by reciting specific structural feature of the recited gene encoding protein from *S. mobaraensis*, because any bacteria may have multiple genes encoding distinct protein with the same enzymatic activity, which should be correlated with its functional feature as recited in the present application, otherwise, one of ordinary skill in

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the art would not be able to practice the claim invention, which requires that one of ordinary skill in the art to know or be provided with guidance for obtaining other transglutaminase genes encoded by *S. mobaraensis*. Such guidance would include how to make in terms of isolation of other genes besides transglutaminase gene disclosed by the applicants having similar activity from *S. mobaraensis* and how to use those genes to make the transformant. The specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification.

For all the reasons above, the examiner finds that amendment of claims and new claims and applicant's arguments do not describe the structural features of claimed genus encompassed by the claims in sufficient detail to overcome the rejection. Therefore, for the reasons above, the rejection is maintained.

Maintained-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Previous rejection of Claims 13-14, 16, 18-19, 20, 22 and 24 under 35 U.S.C. 102(e) as being anticipated by Taguchi et al. (WO 01/29187 A1, "Process for producing microorganism-origin transglutaminase", Ajinomoto Co., Inc., see IDS) is maintained and new claims 31-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Taguchi et al. as the reasons given in previous office action and discussed below. As discussed previously, Taguchi et al. disclose a

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process for producing microorganism-origin (*Streptomyces mobaraensis*) transglutaminase in transformant and the sequence of a transglutaminase (SEQ ID NO: 3) which is 100% identical to SEQ ID NO: 1 and the coding sequence of SEQ ID NO: 2 of the instant application. Taguchi et al. also disclose that gene is derived from *S. mobaraensis* with natural promoter. Taguchi et al. further disclose the cloning the cDNA in expression vector, which includes a transcriptional terminator derived from *Streptomyces azureus* (*tsr* gene comprises terminator) and producing transformant *S. lividans* comprising the expression vector containing the sequence of a transglutaminase gene to produce transglutaminase in high efficiency. Taguchi et al. also mutated the transglutaminase gene and transformed *S. lividans*. New Claims 31-36 are anticipated by Taguchi et al. and are included in this rejection because the DNA of Taguchi et al. would hybridize with SEQ ID NO: 2 at the recited hybridizing conditions because the DNA of Taguchi et al. is 100% identical to the entire coding region of SEQ ID NO: 2 of the instant application.

Applicants argue that Taguchi et al. do not teach a terminator and examiner is incorrect. This is not found persuasive because Taguchi et al. indeed teach using termination signal sequence. The shuttle vector pUJ-MTG, which is used to make transformant, comprises microbial transglutaminase (MTG) gene, that is prepared by combining several vectors including pIJ702, which is streptomyces specific vector contains *tsr* gene, which comprises a streptomyces specific termination signal sequence (*Streptomyces azureus*) (see Pulido et al. Optimization of gene expression in *Streptomyces lividans* by a transcription terminator, NAR 15(10) 1987, p4227-4240). Thus, for the reasons above, the rejection is maintained. However, previous rejection of Claims 15, 17, 21 and 23 under 35 U.S.C. 102(e) as being anticipated by Taguchi et

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al. is withdrawn because the Taguchi et al. do not teach terminator sequence from *S. mobaraensis* transglutaminase gene but rather from *S. azureus* *tsr* gene. Therefore, the rejection is withdrawn.

Maintained-Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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Previous rejection of Claims 1-2, 4, 6-8, 10 and 12 under 35 U.S.C. 103(a) as being unpatentable over Taguchi et al. (WO 01/29187 A1, "Process for producing microorganism-origin transglutaminase", Ajinomoto Co., Inc., see IDS) is maintained and newly added claims 25-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taguchi et al. as reasons discussed in previous office action and is now discussed below. The rejection was explained in the previous office action. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection on obviousness issue.

Applicants argue that the examiner raise the motivation issue by stating that one skilled artisan would have (been) motivated to express the gene of transglutaminase with natural promoter and terminator from *S. mobaraensis* to produce a recombinant strain of same host *S. mobaraensis* to produce transglutaminase in increased level but the stated motivation for this modification of the reference is therefore derived entirely from an assumption that using the same bacterium as the source of the gene and as the host would give increased level" or high efficiency" of expression of the said protein. However, the Examiner has given no basis in the general art for this assumption. Note that MPEP 2143.01 states: obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art." Applicants further argue that according to MPEP 2142: To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to modify the reference or to combine reference teachings. Second, there must be a

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reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not based on applicant's disclosure." Applicant therefore submits that the Examiner has not provided a proper basis for the proposed modification of Taguchi et al. to use transformants of *S. mobaraensis*. Since Taguchi et al. does not disclose or suggest the terminator recited in the present claims, and since the Examiner has not provided a proper motivation to modify Taguchi et al. to use transformants of *S. mobaraensis*, claims 1-12 are not anticipated by and non-obvious over Taguchi et al.

As discussed in the previous office action and above, Taguchi et al. disclose a process for producing microorganism-origin (*S. mobaraensis*) transglutaminase in transformant and the sequence of a transglutaminase (SEQ ID NO: 3) which is 100% identical to SEQ ID NIO: 1 and the coding sequence of SEQ ID NO: 2 of the instant application and any DNA would hybridize with SEQ ID NO: 1 at the recited high stringency hybridizing conditions (claims 25-30). Taguchi et al. also disclose that gene is derived from *S. mobaraensis* with natural promoter. Taguchi et al. further disclose the cloning the cDNA in expression vector and producing transformant *S. lividans* (current invention is making transformant of *S. lividans* and *S. mobaraensis*) comprising the expression vector containing the sequence of a transglutaminase gene to produce transglutaminase in high efficiency. Taguchi et al. already disclose a part of the instant claimed invention but do not disclose transforming *S. mobaraensis* comprising sequence of a transglutaminase gene.

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Regarding, terminator sequence, Taguchi et al. indeed teach using transcriptional termination signal sequence. Taguchi et al teach the use of shuttle vector pUJ-MTG, which is used to make transformant, comprises microbial transglutaminase (MTG) gene, that is prepared by combining several vectors including pIJ702 vector, which is a streptomyces specific vector contains tsr gene. The tsr gene comprises a streptomyces specific termination signal sequence derived from *Streptomyces azureus* (see Pulido et al. Optimization of gene expression in *Streptomyces lividans* by a transcription terminator, NAR 15(10) 1987, p4227-4240). Furthermore, contrary to applicant's arguments a skilled artisan would have been motivated to express the transglutaminase gene of Taguchi et al. in *S. mobaraensis* because native regulatory factors, which are present in *S. mobaraensis* would activate the transcription by acting on natural promoter to produce said transglutaminase protein in increased amounts than other host cell. Therefore, it would have been obvious to transform *S. mobaraensis* as taught by Taguchi et al. Thus, for the reasons above, the rejection is maintained.

Conclusion

No claim is in condition for allowance.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

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will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

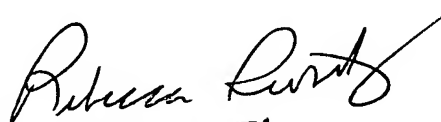
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury, Ph.D. whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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